

WHAT IS CLAIMED IS:

- 1 1. A method for sequencing a terminal portion of an oligomer,
2 comprising:
3 (a) contacting said oligomer with a labeling moiety to covalently attach a
4 label to the terminus of the oligomer and form a labeled oligomer, said labeling moiety
5 comprising at least one element having an atomic number from 17 to 77, with the proviso that
6 said element is other than sulfur or phosphorus;
7 (b) fragmenting said labeled oligomer using an enzymatic, chemolytic or
8 mass spectrometric fragmentation method to produce labeled oligomer fragments; and
9 (c) analyzing said labeled oligomer fragments using a mass spectrometric
10 fragmentation method to determine the sequence of at least two terminal residues.
- 1 2. The method of claim 1, wherein said labeling moiety comprises at least
2 one element of atomic number 35 to 63.
- 1 3. The method of claim 2, wherein said labeling moiety comprises at least
2 one element of atomic number 39 to 58.
- 1 4. The method of claim 2, wherein said labeling moiety comprises at least
2 one element selected from the group consisting of bromine, iodine, europium and yttrium.
- 1 5. The method of claim 4, wherein said element is europium.
- 1 6. The method of claim 4, wherein said element is yttrium.
- 1 7. The method of claim 4, wherein said element is bromine.
- 1 8. The method of claim 4, wherein said element is iodine.
- 1 9. The method of claim 1, wherein said oligomer is selected from the
2 group consisting of a protein, an oligonucleotide, an oligosaccharide and a lipid.
- 1 10. The method of claim 9, wherein said oligomer is an oligonucleotide.
- 1 11. The method of claim 9, wherein said sequence is at least three residues.
- 1 12. The method of claim 9, wherein said sequence is at least four residues.

1 13. The method of claim 1, wherein several oligomers, each labeled with a
2 different number of mass defect elements are mixed prior to said fragmenting or analyzing
3 step.

1 14. A method for sequencing a portion of an oligomer in an oligomer
2 mixture, said method comprising:

3 (a) contacting said oligomer mixture with a terminus labeling moiety to
4 covalently attach a label to the terminus of said oligomer and form a labeled oligomer
5 mixture, said terminus labeling moiety comprising at least one element having an atomic
6 number from 17 to 77, with the proviso that said element is other than sulfur or phosphorus;

7 (b) separating individual labeled oligomers in said labeled oligomer mixture;
8 and

9 (c) analyzing said individual labeled oligomers from step (b) by a mass
10 spectrometric method to determine the sequence of at least two terminus residues.

1 15. A method in accordance with claim 14, wherein said element has an
2 atomic number of from 35 to 63.

1 16. A method in accordance with claim 14, wherein said element has an
2 atomic number of from 39 to 58.

1 17. A method in accordance with claim 14, wherein said element is
2 selected from the group consisting of bromine, iodine, europium and yttrium.

1 18. A method in accordance with claim 14, further comprising a step prior
2 to step (a) of isolating a group of oligomers from a biological sample.

1 19. A method in accordance with claim 18, wherein said biological sample
2 is from a diseased tissue sample.

1 20. A method in accordance with claim 18, wherein said biological sample
2 is from a healthy tissue sample.

1 21. A method in accordance with claim 14, wherein said separating is
2 conducted by at least one method of capillary electrophoresis of the labeled oligomer
3 mixture.

1 22. A method in accordance with claim 14, wherein said mass
2 spectrometric method uses ESI-TOF MS.

1 23. A method for structure and function analysis of an oligomer having a
2 plurality of residues, said method comprising:

3 (a) contacting said oligomer with a mass defect labeling reagent to
4 differentially label exposed residues and unexposed residues and produce a differentially
5 labeled oligomer, wherein said mass defect labeling reagent comprises at least one element
6 having an atomic number of from 17 to 77 that is other than sulfur or phosphorus;

7 (b) analyzing said differentially labeled oligomer by a mass spectrometric
8 method to determine sequences of said oligomer that are exposed in the three-dimensional
9 structure and sequences of said oligomer that are unexposed in the three-dimensional
10 structure.

1 24. A method in accordance with claim 23, wherein said oligomer is a
2 protein, a nucleic acid, or an oligosaccharide.

1 25. A method in accordance with claim 23, wherein said mass defect
2 labeling reagent comprises at least one element of atomic number 35 to 63.

1 26. A method in accordance with claim 26, wherein said mass defect
2 labeling reagent is bromine and said oligomer is a protein.

1 27. A method in accordance with claim 23, wherein said mass defect
2 labeling reagent comprises at least one element of atomic number 39 to 58.

1 28. A method in accordance with claim 23, wherein said differentially
2 labeled oligomer is fragmented by enzymatic or chemolytic methods prior to step (b).

1 29. A method in accordance with claim 23, wherein said oligomer is a
2 protein, said mass defect is bromine or iodine and said exposed residues comprises a portion
3 of the tyrosine residues present in said protein.

1 30. A method in accordance with claim 23, wherein said mass
2 spectrometric method uses ESI-TOF MS.

1 31. A method in accordance with claim 29, wherein said mass
2 spectrometric method uses ESI-TOF MS.

1 32. A method for sequencing the terminal portion of an oligomer,
2 comprising:

3 (a) contacting a first sample of said oligomer with a labeling moiety to
4 covalently attach a label to the terminus of the oligomer and form a labeled oligomer, said
5 labeling moiety having one element with an atomic number from 17 to 77, with the proviso
6 that said element is other than sulfur or phosphorus;

7 (b) contacting a second sample of said oligomer with a labeling moiety to
8 covalently attach a label to the terminus of the oligomer and form a labeled oligomer, said
9 labeling moiety having two elements with an atomic number from 17 to 77, with the proviso
10 that said elements are other than sulfur or phosphorus;

11 (c) optionally, repeating step (b) from one to three times with additional
12 samples, wherein the labeling moieties have three, four or five elements, respectively, with an
13 atomic number from 17 to 77, with the proviso that said elements are other than sulfur or
14 phosphorus;

15 (d) mixing the labeled oligomers from steps (a) through (c);

16 (e) fragmenting said labeled oligomers using an enzymatic, chemolytic or
17 mass spectrometric fragmentation method to produce labeled oligomer fragments; and

18 (f) analyzing said labeled oligomer fragments using a mass spectrometric
19 fragmentation method to determine the sequence of at least two terminal residues.

1 33. The method of claim 32, wherein each of said elements has an atomic
2 number of from 35 to 63.

1 34. The method of claim 32, wherein each of said elements has an atomic
2 number of from 39 to 58.

1 35. The method of claim 32, wherein each of said elements is selected
2 from the group consisting of bromine, iodine, europium and yttrium and said oligomer is a
3 protein.

1 36. The method of claim 32, wherein each of said elements is selected
2 from the group consisting of bromine, iodine, europium and yttrium and said oligomer is an
3 oligonucleotide.

1 37. The method of claim 32, wherein each of said elements is selected
2 from the group consisting of bromine, iodine, europium and yttrium and said oligomer is an
3 oligosaccharide.

1 38. A method for sequencing a portion of an oligomer, comprising:
2 (a) fragmenting aliquots of said oligomer using one or more specific
3 enzymatic or chemolytic fragmentation methods to produce oligomer fragments, wherein a
4 different fragmentation method is applied to each aliquot;
5 (b) contacting a first aliquot of oligomer fragments with a first labeling
6 moiety to covalently attach said first labeling moiety to the terminus of the oligomer
7 fragments and form labeled oligomer fragments, said first labeling moiety having one
8 element with an atomic number from 17 to 77, with the proviso that said element is other than
9 sulfur or phosphorus;
10 (c) optionally contacting the other aliquots of oligomer fragments with other
11 distinct labeling moieties to covalently attach said distinct labeling moieties to the termini of
12 the oligomer fragments and form labeled oligomer fragments, said distinct labeling moiety
13 having two or more elements with an atomic number from 17 to 77, with the proviso that said
14 elements are other than sulfur or phosphorus;
15 (d) optionally mixing the aliquots of labeled oligomer fragments; and
16 (e) analyzing said labeled oligomer fragments using a mass spectrometric
17 fragmentation method to determine the sequence of at least two residues of said oligomer.

1 39. A method in accordance with claim 38, wherein said oligomer is a
2 lipid.

1 40. A method in accordance with claim 38, wherein said oligomer is a
2 protein.

1 41. A method in accordance with claim 38, wherein said oligomer is a
2 nucleic acid.

1 42. A method in accordance with claim 38, wherein said oligomer is an
2 oligosaccharide.

1 43. A method in accordance with claim 38, wherein said elements have an
2 atomic number of from 35 to 63.

1 44. A method in accordance with claim 43, wherein said elements have an
2 atomic number of from 39 to 58.

1 45. A method for comparing the relative abundances of analytes from two
2 or more samples, comprising:

3 (a) contacting the analytes of the first sample with with a labeling moiety to
4 covalently attach a label to the analytes and form labeled analytes, said labeling moiety
5 having one element with an atomic number from 17 to 77, with the proviso that said element
6 is other than sulfur or phosphorus;

7 (b) contacting the analytes of subsequent samples with labeling moieties to
8 covalently attach labels to the analytes in each sample, wherein the labeling moieties used for
9 each subsequent sample contain an additional element with an atomic number from 17 to 77,
10 with the proviso that said elements are other than sulfur or phosphorus;

11 (c) mixing the aliquots of labeled analytes; and

12 (d) analyzing said labeled analytes using a mass spectrometric fragmentation
13 method to determine the relative abundances of one or more of the analytes between the
14 samples.

1 46. A method in accordance with claim 45, wherein said elements have an
2 atomic number of from 35 to 63.

1 47. A method in accordance with claim 45, wherein said elements have an
2 atomic number of from 39 to 58.

1 48. A method for tagging the elements of chemical libraries, either during
2 synthesis or screening, comprising;

3 (a) contacting a root tag with a labeling moiety to covalently attach a label to
4 the root tag and form a labeled tag, said labeling moiety having one element with an atomic
5 number from 17 to 77, with the proviso that said element is other than sulfur or phosphorus;

6 (b) optionally, contacting a root with additional labeling moieties to
7 covalently attach additional labels to the root tag and form a multiply labeled tag, said
8 labeling moiety having one element with an atomic number from 17 to 77, with the proviso
9 that said element is other than sulfur or phosphorus; and
10 (c) analyzing the labeled tag by mass spectrometric methods to determine
11 both its mass and the number of elements with an atomic number from 17 to 77, such that the
12 mass and number of elements identifies the chemical processes to which the specific
13 chemical of the library has been exposed and the identity of the chemical from the library.

1 49. A method in accordance with claim 48, wherein said elements have an
2 atomic number of from 35 to 63.

1 50. A method in accordance with claim 48, wherein said elements have an
2 atomic number of from 39 to 58.

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